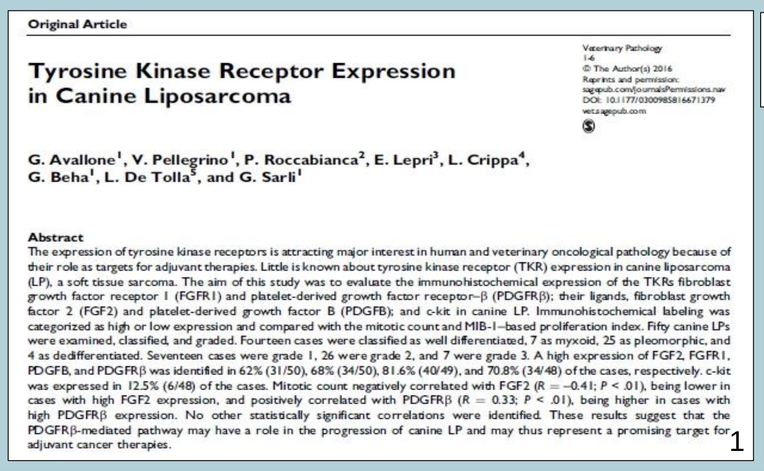
DIPARTIMENTO DI SCIENZE MEDICHE VETERINARIE

Dottoranda XXXI ciclo
Area: Sanità Pubblica
Valeria Pellegrino
Tutor: Prof. Giuseppe Sarli

PhD project: "Canine soft tissue sarcomas: identification of histotypes and pathological variables, their biological behaviour and targets for adjuvant therapies"

Adipose differentiation



Original Article

Tyrosine Kinase Receptor Expression in Canine Liposarcoma

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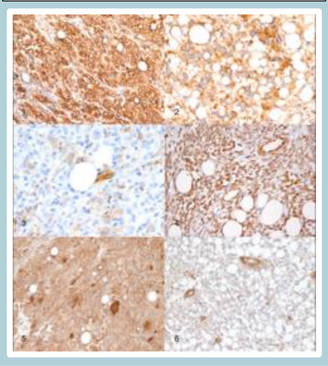
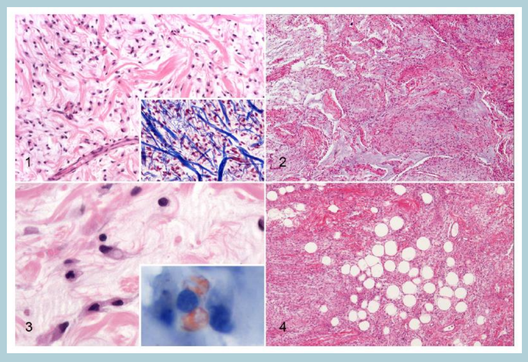
Abstract
The expression of tyrosine kinase receptors is attracting major interest in human and veterinary oncological pathology because of their role as targets for adjuvant therapies. Little is known about tyrosine kinase receptor (TKR) expression in canine liposarcoma (LP), a soft tissue sarcoma. The aim of this study was to evaluate the immunohistochemical expression of the TKRs fibroblast growth factor receptor 1 (FGFR1) and platelet-derived growth factor receptor–β (PDGFRβ); their ligands, fibroblast growth factor 2 (FGF2) and platelet-derived growth factor B (PDGFB); and c-kit in canine LP. Immunohistochemical labeling was categorized as high or low expression and compared with the mitotic count and MIB-1–based proliferation index. Fifty canine LPs were examined, classified, and graded. Fourteen cases were classified as well differentiated, 7 as myxoid, 25 as pleomorphic, and 4 as dedifferentiated. Seventeen cases were grade 1, 26 were grade 2, and 7 were grade 3. A high expression of FGF2, FGFR1, PDGFB, and PDGFRβ was identified in 62% (31/50), 68% (34/50), 81.6% (40/49), and 70.8% (34/48) of the cases, respectively. c-kit was expressed in 12.5% (6/48) of the cases. Mitotic count negatively correlated with FGF2 ($R = -0.41$; $P < .01$), being lower in cases with high FGF2 expression, and positively correlated with PDGFRβ ($R = 0.33$; $P < .01$), being higher in cases with high PDGFRβ expression. No other statistically significant correlations were identified. These results suggest that the PDGFRβ-mediated pathway may have a role in the progression of canine LP and may thus represent a promising target for adjuvant cancer therapies.

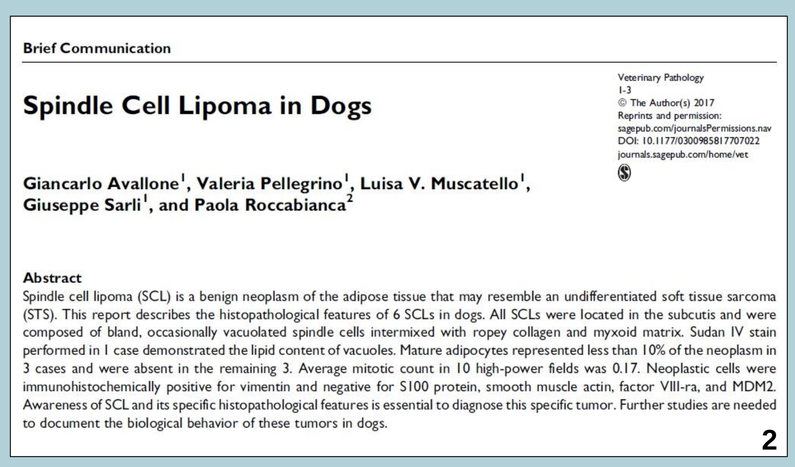
1

Immunohistochemical expression of TKR in canine liposarcoma



Histological features of canine spindle cell lipoma





Brief Communication

Spindle Cell Lipoma in Dogs

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Giancarlo Avallone[1], Valeria Pellegrino[1], Luisa V. Muscatello[1], Giuseppe Sarli[1], and Paola Roccabianca[2]

Abstract
Spindle cell lipoma (SCL) is a benign neoplasm of the adipose tissue that may resemble an undifferentiated soft tissue sarcoma (STS). This report describes the histopathological features of 6 SCLs in dogs. All SCLs were located in the subcutis and were composed of bland, occasionally vacuolated spindle cells intermixed with ropey collagen and myxoid matrix. Sudan IV stain performed in 1 case demonstrated the lipid content of vacuoles. Mature adipocytes represented less than 10% of the neoplasm in 3 cases and were absent in the remaining 3. Average mitotic count in 10 high-power fields was 0.17. Neoplastic cells were immunohistochemically positive for vimentin and negative for S100 protein, smooth muscle actin, factor VIII-ra, and MDM2. Awareness of SCL and its specific histopathological features is essential to diagnose this specific tumor. Further studies are needed to document the biological behavior of these tumors in dogs.

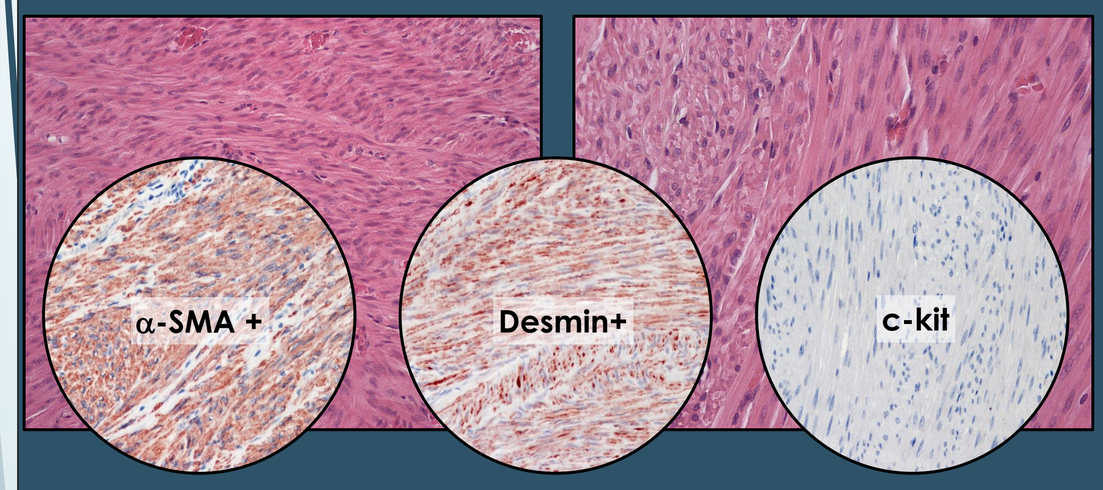
2

Smooth muscle tumors: Leiomyoma VS Leiomyosarcoma

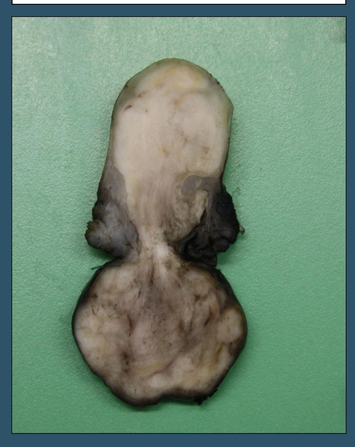
In veterinary medicine a real distinction between this two entity are lacking and it's based on mitotic activity, cellular atypia and amount of necrosis.
Aims → describe clinico-pathological features of canine SMTs and identify potential criteria to differentiate benign from malignant one.
Sixty-eight SMTs were collected in 67 dogs. 18 cases were classified as UMP (uncertain malignant potential) because of:
- well-differentiated
- slightly higher MC than leiomyomas
- some degree of cellular atypia and necrosis

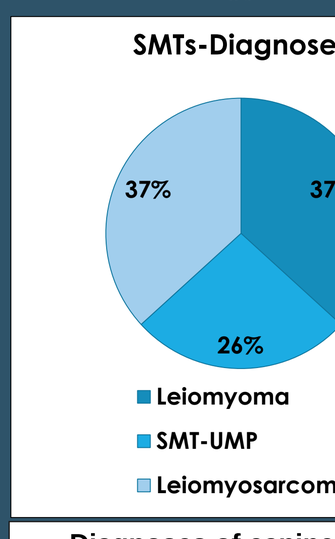
We suggest to use LI with a cut-off of 5 to distinguish leiomyomas from leiomyosarcomas when histology alone Is not sufficient.

Inclusion criteria:
Morphology suggestive of smooth muscle differentiation.
IHC reactivity: a-SMA and/or Desmin +, c-kit-

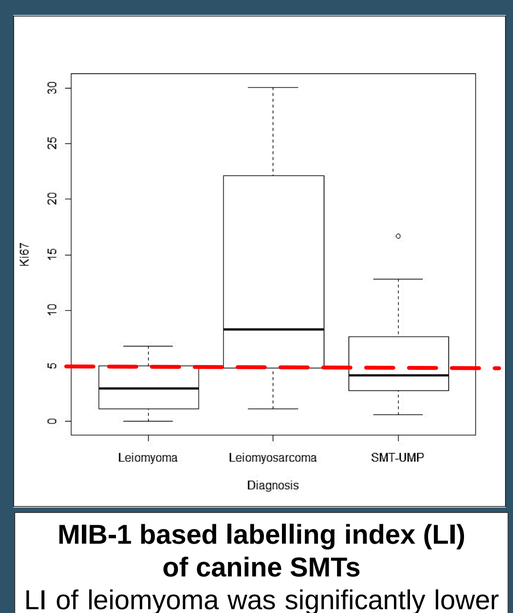


Leiomyosarcoma of the urinary bladder transpassing the vescical wall.





Diagnoses of canine SMTs
The number of benign and malignant SMTs were equivalent. SMTs-UMP were 26%



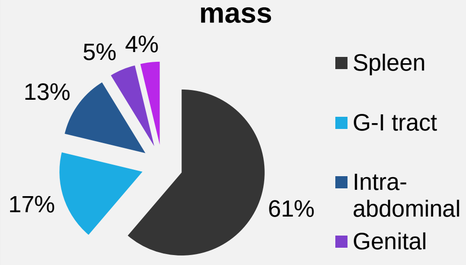
MIB-1 based labelling index (LI) of canine SMTs
LI of leiomyoma was significantly lower (than LI of leiomyosarcoma ($p<0.01$).
LI was ≤5 (broken line) in 76% of leiomyomas and in 28% of leiomyosarcoma, and in 12/18 SMT-UMP (67%).

3

Poster award ESVP congress 7-10 Sep 2016 Bologna

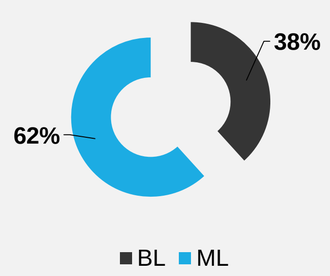
Clinicopathological features of canine intra-abdominal masses: 80 cases
Epidemiological data on canine abdominal masses are fragmentary and focused on specific diagnoses and site.
Aims → describe the epidemiology, distribution and diagnoses of canine abdominal masses.

Site of occurrence of canine intra-abdominal mass



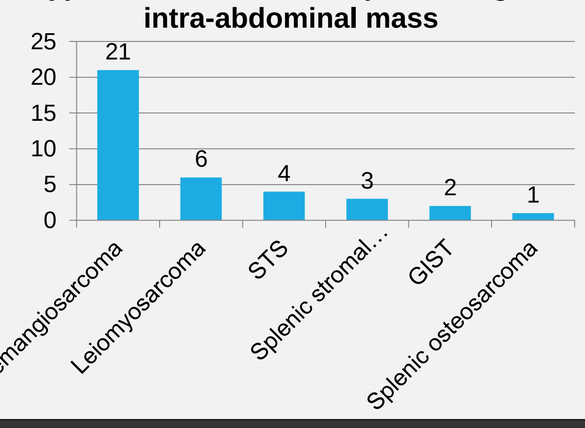
Spleen, GI tract and intra-abdominal without connection with any organ were the 3 most represented sites.

Frequency of Benign and Malignant lesions



The majority of the lesions (62%) were malignant.

Type of canine sarcoma presenting as intra-abdominal mass



The majority of the malignant lesions were of mesenchymal origin, followed by leukocytic, and were represented mainly by splenic hemangiosarcoma and gastrointestinal leiomyosarcoma

4

Histopathological assessment of disease target organs in a mouse model of progeria (LMNA G609G/G609G)

Hutchinson-Gilford Progeria syndrome is a fatal disorder characterized by accelerated aging caused by an LMNA gene mutation, which elicits production of progerin, a mutant lamin A precursor.
We collected 41 mice of this strain further genotyped as 5 wild type (WT), 27 Heterozygotes (Het.) and 9 Homozygotes (Homo.) as for the mutation.
Aims → assess the target organs and their changes at the clinical end point stage.
Results → The most frequently affected organs were lung, skin, large arteries, spleen, bones. Genotype-associated lesions are shown in table 2.
Discussion → The findings reflect most of the lesions occurring in the human disease (weight loss, lipodystrophy, dermic and cardiovascular changes, bone disorders) [4]. Genotype-associated changes including atrophy of the adipose tissue in the subcutis, catagen follicles and artheriopathy can be quantified to evaluate severity of disease at end point or the effectiveness of therapy in a pharmacological trial.

Genotype/lesions	Kyphosis of the cervico-thoracic spine	Alopecia associated with reduction in number of follicles and dermal fibrosis	Hypoplasia/atrophy of the adipose tissue of the subcutis	Reduction of cells in the tunica media of aorta paralleled by an increase of slightly eosinophilic intramural substance
WT	0	0/5	1/5	0/4
Het	27/27	27/27	27/27	14/21
Homo	9/9	8/9	8/9	7/7

5

References: 1) Avallone G, Pellegrino V, Roccabianca P, Lepri E, Crippa L, Beha G, De Tolla L, Sarli G. Tyrosine Kinase Receptor Expression in Canine Liposarcoma. Vet Pathol. 2017 Mar;54(2):212-217; 2) Avallone G, Pellegrino V, Muscatello LV, Sarli G, Roccabianca P. Spindle Cell Lipoma in Dogs. Vet Pathol. 2017 Jan 1:300985817707022. doi:10.1177/0300985817707022; 3) Avallone, G., et al. "Characterization of Canine Smooth Muscle Tumours: Pilot Study of 68 Cases." , J. Comp. Path. 2017, Vol. 156;.4) G Avallone, P Valenti, V Pellegrino, B Brunetti, E Zambonz and G Sarli Clinicopathological features of 80 canine abdominal masses., J. Comp. Path. 2017, Vol. 156;5) Gonzalo et al.: Hutchinson-Gilford Progeria Syndrome: A premature aging disease caused by LMNA gene mutations. Ageing Res Rev. 33:18-29, 2017.